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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/602,024	06/24/2003	Bradley G. Thompson	16596-001001	7648

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FISH & RICHARDSON P.C.
PO BOX 1022
MINNEAPOLIS, MN 55440-1022

EXAMINER	
BROWN, TIMOTHY M	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 12/30/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/602,024	THOMPSON ET AL.	
	Examiner	Art Unit	
	Timothy M. Brown	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 September 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-25,27,28 and 30-33* is/are pending in the application.

4a) Of the above claim(s) *7,14,16-22,27,28 and 30-33* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,8-13,15 and 23-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This Final Office Action is responsive to the communication received September 30, 2005. Claims 1-25, 27, 28 and 30-33 are pending. Claims 1-6, 8-13, 15 and 23-25 are under examination. Claims 7, 14, 16-22, 27, 28 and 30-33 are withdrawn.

Election/Restrictions

The elected invention is a method for detecting ras-activated neoplastic cells comprising contacting a sample of cells with a serotype 3 Dearing strain reovirus, and identifying the sample of cells as ras-activated neoplastic cells if the reovirus can replicate in the sample. This invention corresponds to Group I, subgroup i as defined in the Office Action mailed June 1, 2005 ("the Office Action"). Note that subgroup i consists of subgroups i, iii, and xv from the Restriction Requirement mailed March 8, 2005; subgroups iii and xv were rejoined with elected subgroup i in response to Applicants' remarks.

Claim 27 was omitted from the claim listing in the Office Action's restriction requirement. Claim 27 recites the viruses listed under subgroups iv-x. Thus, claim 27 clearly belongs to subgroups iv-x.

The restriction requirement is made final for the reasons of record.

Claims 25 and 28 are directed to inventions that are independent or distinct from the invention originally claimed. The elected invention is a method for detecting a *ras-activated neoplasm*. Claims 25 and 28 however recite methods for detecting neoplasms that are activated by interferon resistance or a deficiency in p53, Rb or PKR. These methods are unrelated to the elected invention because (i) they are not disclosed as capable of use with the elected invention, and (ii) they have different functions based on their detecting of different cell populations.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, the claimed methods for detecting neoplasms based on interferon resistance or the claimed deficiencies are withdrawn from consideration. See 37 CFR 1.142(b) and MPEP § 821.03.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 23-25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims are indefinite in the recitation of "provided the oncolytic virus is not an adenovirus." One skilled in the art would not understand whether this language indicates that (i) the execution of the method steps are conditioned on the use of adenovirus, or (ii) the method steps are only performed using a non-adenovirus. Appropriate correction is required.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claim 23 is rejected under 35 U.S.C. 102(e) as being anticipated by Roberts et al. (US 200-/0165465 A1) ("Roberts").

Applicants claim a method for diagnosing the presence of a neoplasm in a mammal comprising contacting a sample of cells from the mammal with an oncolytic virus, wherein replication of the onclytic virus in the cells indicates the presence of a neoplasm. The oncolytic virus may be any virus except adenovirus.

Roberts discloses a differential cytotoxicity assay wherein Newcastle disease virus (NDV) is exposed to tumor cells under conditions which allow the NDV to replicate. Based on this disclosure, Roberts anticipates the subject matter of claim 23. Note that indicating the presence of a neoplasm is inherent to Robert's teachings because NDV is only capable of replicating in tumor cells. Thus, NDV's replication in an isolated cell population necessarily indicates the presence of a neoplasm.

Claim Rejections - 35 USC § 103

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-6, 8-13, 15, 24 and 25 **are rejected under 35 U.S.C. 103(a) as being unpatentable over "Fueyo" (U.S. Pat. App. No. US2003/0138405 A1) in view of "Norman" (Norman, K.L. "*Reovirus as a novel oncolytic agent*" J. Clin. Invest. (April 2000) Vol. 105, No. 8, 1035-1038).**

Applicants claim a method for diagnosing a ras-activated neoplasm in a human comprising the steps of providing a sample of cells from the human, contacting the sample of cells with serotype 3 Dearing strain reovirus, determining the ability of the reovirus to replicate in the sample, and identifying the animal as having a ras-activated neoplasm if the reovirus can replicate in the sample. The method further provides that the biological sample is from a neoplasm in the central nervous system. Fueyo discloses a method for diagnosing an Rb- and/or p53-type neoplasm comprising the steps of providing a sample of human brain tissue (¶ 0238), exposing the sample to an oncolytic adenovirus (¶ 0240), and indicating the presence of an Rb- and/or p53-type neoplasm based on the ability of the adenovirus to replicate in the brain tissue sample (Id.). Fueyo does not expressly disclose a ras-activated neoplasm, or contacting the sample with reovirus. However, Norman teaches that reovirus replication is restricted to neoplasms with a ras-activated phenotype, and that normal cell phenotypes are resistant to reovirus. In light of Norman, one skilled in the art would appreciate that Fueyo's method could be practiced with reovirus in order to diagnose ras-activated neoplasms. Moreover, this combination would enjoy a reasonable expectation of success since both Fueyo and Norman rely on the same principles. That is, both methods diagnose a neoplasm based on the replication of a virus that is selective for a specific neoplastic phenotype.

Claims 1-6, 8-13, 15, 24 and 25 **are rejected under 35 U.S.C. 103(a) as being unpatentable over "Fueyo" (U.S. Pat. App. No. US2003/0138405 A1) in view of *"Strong" (Strong, J.E.* "The molecular basis of viral oncolysis: usurpation of the Ras signaling pathway by reovirus" *EMBO (1998) Vol. 17, No. 12, 3351-3362).***

Applicants claim a method for diagnosing a ras-activated neoplasm in a human comprising the steps of providing a sample of cells from the human, contacting the sample of cells with serotype 3 Dearing strain reovirus, determining the ability of the reovirus to replicate in the sample, and identifying the animal as having a ras-activated neoplasm if the reovirus can replicate in the sample. The method further provides that the biological sample may comprise a neoplasm from the central nervous system. Fueyo teaches all the limitations noted above. Fueyo does not expressly teach a ras-activated neoplasm, or contacting the sample with reovirus. However, Norman overcomes this deficiency by teaching that serotype 3 Dearing strain reovirus selectively replicates in cells having a ras-activated phenotype (see e.g. abstract). This teaching would have motivated one skilled in the art to modify Fueyo's method to include exposing the sample to reovirus in order to identify neoplasms having a ras-activated phenotype. One skilled in the art would have a reasonable expectation of success applying reovirus to Fueyo's method because like the oncolytic adenovirus in Fueyo, Strong's reovirus only replicates in cells having a neoplastic phenotype. Therefore, at the time of Applicants' invention, it would have been obvious to modify Fueyo with Strong teachings in order to diagnose the presence of ras-activated neoplasms.

Response to Arguments

35 U.S.C. 103(a) - Fueyo in view of Norman

Applicant argues the rejection of the claims as obvious over Fueyo (US 2003/0138405) in view of Norman (J. Clin. Invest. (April 2000) Vol. 105, No. 8, 1035-1038) is improper in view of the restriction requirement. Applicants reason that because the restriction requirement held that performing the claimed method using adenovirus was patentably distinct from performing the method with reovirus. However, this argument is not persuasive because the scope of the claimed adenovirus differs from the scope of the prior art adenovirus. The claimed adenovirus incorporates the VA1 mutation unlike the adenovirus of Fueyo.

Applicants urge that the Fueyo does not teach or suggest diagnosing ras-activated neoplasms in an animal because Fueyo lacks taking a sample from an animal. The Examiner respectfully disagrees. Fueyo expressly provides that its method is used to characterize a tumor cell phenotype (¶¶ 0017, 0026). Fueyo also discloses "determining a cancer or tumor cell *in a patient* has a defective or mutated Rb pathway . . . " (¶ 0030). Fueyo therefore discloses taking a sample from an animal.

The suggestion of detecting *ras-activated* neoplasms is found in Norman. Norman states that type 3 Dearing reovirus is able to differentiate between Ras-activated and non-Ras-activated cell phenotypes. The knowledge generally available at the time of filing, and indeed Fueyo, taught that viruses selective for a particular phenotype can be used to classify tumors. Thus, Norman's teaching of the selectivity of reovirus made it apparent that reovirus could be used to detect ras-activated neoplasms. Accordingly, it would have been obvious to combine Fueyo and Norman to arrive at the claimed invention.

35 U.S.C. 103(a) - Fueyo in view of Strong

Applicants argue the rejection of the claims under Fueyo in view of Strong is improper in view of the restriction requirement. Applicants also argue Fueyo does not teach or suggest the use of reoviruses. The Examiner respectfully disagrees as discussed above.

Applicants argue Strong teaches away from identifying a ras-activated neoplasm because Strong knows the cell sample comprises ras-activated cells prior to contacting the cell sample with virus. The Examiner respectfully disagrees.

Where the teachings of two or more prior art references conflict, the examiner must weigh the power of each reference to suggest solutions to one of ordinary skill in the art,

considering the degree to which one reference might accurately discredit another. *In re Young*, 927 F.2d 588, 18 USPQ2d 1089 (Fed. Cir. 1991).

Here, Fueyo teaches classifying neoplasms based on a virus' ability to selectively replicate in a cell sample. Strong on the other hand demonstrates that reovirus only replicates in ras-activated neoplastic cells. The fact that Strong used a cell line known to be ras-activated to identify the selectivity of reovirus, by itself, does not discredit the combination of Strong and Fueyo. The main conclusion of Strong was that reovirus selectively replicates in ras-activated cells. Morever, the skilled artisan would appreciate that cells known to be ras-transformed cells (i.e. positive controls) would be required to show that reovirus selectively replicates in ras-activated cells. Thus, Strong's teaching of ras-activated positive controls does not teach away from Strong's combination with Fueyo.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Timothy M. Brown whose telephone number is (571) 272-0773. The examiner can normally be reached on Monday - Friday, 8am - 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on (571) 272-0902. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Timothy M. Brown
Examiner
Art Unit 1648

tmb